JOURNAL OF BONE AND MINERAL RESEARCH
Volume 12, Number 8, 1997
Blackwell Science, Inc.

Clinical Vignette

Long-Term Aminobisphosphonate Treatment of Fibrous Dysplasia: Spectacular Increase in Bone Density

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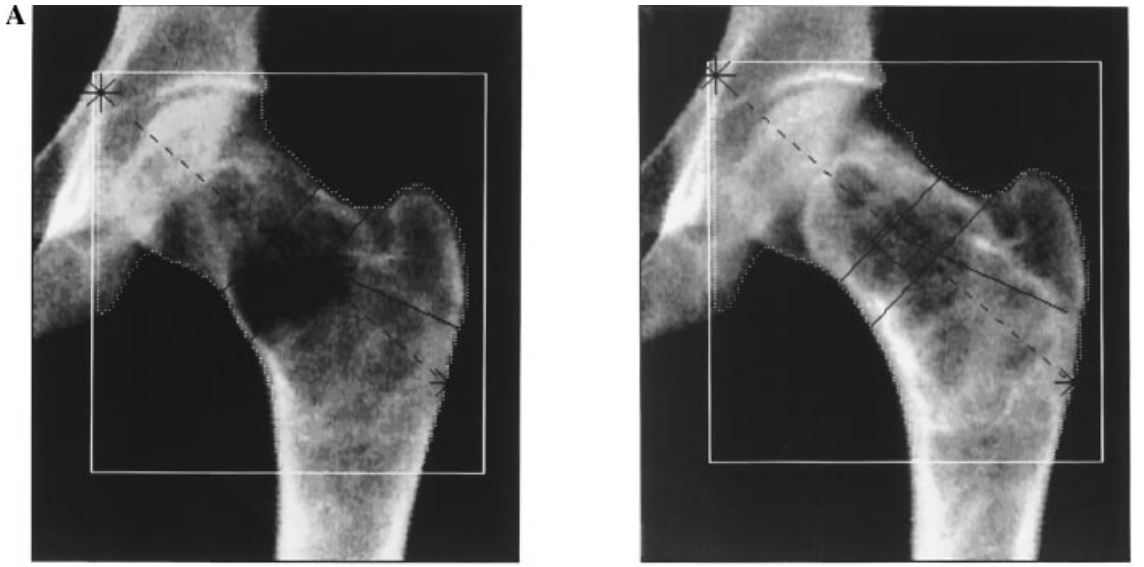
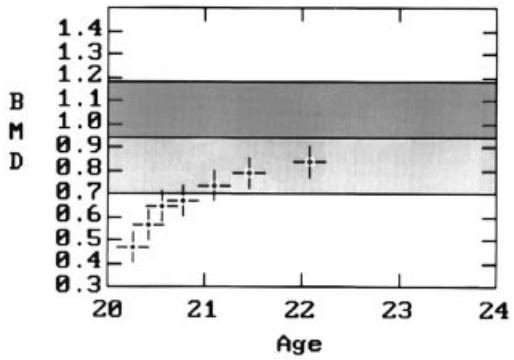
THE MCCUNE-ALBRIGHT SYNDROME is characterized by sexual precocity, large and rough-bordered café-au-lait spots, and polyostotic fibrous dysplasia due to the mosaic distribution of an activating mutation of the $G_s\alpha$ gene in endocrine and nonendocrine tissues.[1,2] In bone, this mutation causes overactive cAMP generation and proliferation of osteoblast progenitors in the bone marrow stroma leading to increased IL-6 synthesis, high levels of c-*fos* expression, and increased numbers of osteoclasts.[3,4] At the advancing margins of the bone lesions, these abnormally stimulated osteoclasts cause expansion of the bony lesions, pain, and pathological fractures.[5]



DATE	Bone-Specific Alk Phos (n=3-21 ng/mL)	N-telo (n=<30 pM BCE/μM creatinine)	BMD Neck	BMD Troch	BMD Ward's	BMD Total Proximal Femur
7/19/95	68	330	0.208	0.429	0.112	0.462
9/15/95		90	0.292	0.486	0.198	0.556
11/06/95		222	0.381	0.557	0.218	0.637
12/13/95		289				
1/24/96		188	0.434	0.519	0.326	0.662
3/96		108				
5/20/96		131	0.517	0.538	0.354	0.730
9/30/96	37	136	0.609	0.575	0.427	0.783
5/16/97		137	0.690	0.623	0.448	0.831



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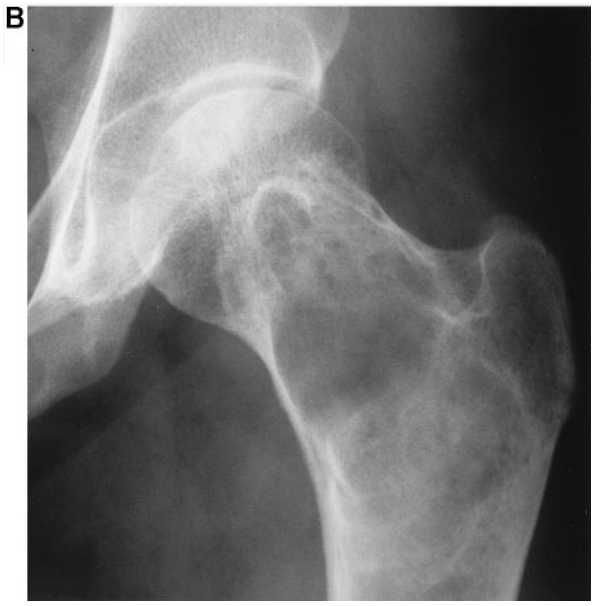

X-ray of the hip shows the ground-glass appearance of the destructive lesion. Note how well the image was captured by the DEXA study in A.

In July of 1995, a 22-year-old white woman presented with the McCune-Albright syndrome and severe pain in her left hip that required her to use crutches. DEXA of the hip (A) and plain films (B) showed an expanding lesion with a thin cortex and a profound decrease in bone mineral density (BMD). She was treated with four 90 mg infusions of intravenous pamidronate given at three to four week intervals from July to September 1995 and a calcium supplement. Relief of pain and increased BMD (A) were accompanied by decreased urinary excretion of the N-telopeptide of type I collagen of bone. In December 1995, pain still interfered with ambulation and the N-telopeptide excretion had increased, prompting the use of oral alendronate therapy. With 10 mg/day, the N-telopeptide excretion decreased, and by September 1996, BMD continued to increase. By February 1997, the patient was pain free; internal and external rotation, flexion, and extension of the left hip were normal, as was her unaided gait. In May 1997, total proximal femoral BMD had increased 158% and the lesion showed marked cortical thickening and refilling from the margins (A). Early fractures and deformities typical of the McCune-Albright syndrome need not occur since this previously medically untreatable bone disease is now amenable to aminobisphosphonate therapy.[6]

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